IN THE CLAIMS

COMPLETE LISTING OF ALL CLAIMS, WITH MARKINGS AND STATUS IDENTIFIERS
(Currently amended claims showing deletions by ~~strikethrough~~ and additions by underlining)

This listing of claims will replace all prior versions and listings of the claims in the application.

Listing of Claims:

1. (original) A method for detecting or determining one or more forms of Factor XIIa in a sample, which comprises carrying out a procedure that is capable of detecting or determining the form or forms of Factor XIIa under investigation in preference to other forms of Factor XIIa.

2. (original) A method as claimed in claim 1, which comprises detecting or determining the form or forms of Factor XIIa under investigation by means of an assay that enables determination of the form or forms of Factor XIIa under investigation in preference to other forms of Factor XIIa.

3. (original) A method as claimed in claim 1, which method comprises separating the form or forms of Factor XIIa under investigation from other forms of Factor XIIa and detecting or determining the separated form or forms of Factor XIIa.

4. (currently amended) A method as claimed in claim 3, wherein the detection or determination of the separated form or forms of Factor XIIa is by means of an assay that enables determination of the form or forms of Factor XIIa under investigation in preference to other forms of Factor XIIa ~~as defined in claim 2~~.

5. (original) A method as claimed in claim 1, which comprises contacting the sample with a labeled antibody that is capable of binding to the form or forms of Factor XIIa under investigation and that is optionally also capable of binding to other forms of Factor XIIa, separating the form or forms of Factor XIIa under investigation from other form, and detecting or determining the form or forms of Factor XIIa under investigation.

6. (currently amended) A method as claimed in claim 3 ~~any one of claims 3 to 5~~, wherein the form or forms of Factor XIIa under investigation is/are separated from other forms of Factor XIIa on the basis of the physical, chemical or immunological properties thereof.

7. (original) A method as claimed in claim 6, wherein the form or forms of Factor XIIa under investigation is/are separated from other forms of Factor XIIa using a chromatographic, flow cytometric or ultracentrifugation procedure, optionally followed by assessment of the enzymatic activity or immunological properties of the separated material.

8. (currently amended) A method as claimed in claim 6, wherein the form or forms of ~~of~~ Factor XIIa under investigation is/are separated by immunoaffinity chromatography using an antibody capable of binding to the form or forms of Factor XIIa under investigation, optionally followed by assessment of enzymatic activity or immunological properties of the separated material.

9. (currently amended) A method as claimed in claim 6 ~~claim 7 or claim 8~~, wherein the separation procedure is carried out under conditions such that the form or forms of Factor XIIa is/are not disrupted.

10. (currently amended) A method as claimed in claim 1 ~~any one of claims 1 to 9~~, wherein the sample is a sample of a body fluid or body tissue.

11. (currently amended) A method as claimed in claim 10, wherein the body fluid is blood, plasma, cerebrospinal fluid, or serum.

12. (currently amended) A method as claimed in claim 10, wherein the body fluid is urine, ~~cerebrospinal fluid,~~ saliva, or tears.

13. (currently amended) A method as claimed in claim 1~~any one of claims 1 to 12~~, wherein the form of Factor XIIa under investigation is cellular Factor XIIa.

14-16. Please cancel.

17. (currently amended) A method as claimed in claim 1~~in any one of claims 1 to 12~~, wherein the form of Factor XIIa under investigation is lipid bound Factor XIIa.

18-21. Please cancel.

22. (currently amended) A method as claimed in claim 1~~any one of claims 1 to 12~~, wherein the form or forms of Factor XIIa under investigation is any one or more of complexes comprising two or more molecules of Factor XIIa, Factor XIIa associated with low affinity binding partners, and Factor XIIa associated with high affinity binding partners.

23-25. Please cancel.

26. (currently amended) A method as claimed in claim 2 ~~claim 25~~, wherein the assay is an immunoassay that is capable of detecting or determining the form or forms of Factor XIIa under investigation preferentially relative to other forms of Factor XIIa.

27. (original) A method as claimed in claim 26, wherein the assay comprises the use of an antibody that is capable of binding to the form or forms of Factor XIIa under investigation.

28. (original) A method as claimed in claim 27, wherein the antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

29. Please cancel.

30. (original) A method as claimed in claim 29, wherein the antibody is radiolabelled.

31-32. Please cancel.

33. (currently amended) A method as claimed in claim 26 ~~any one of claims 25 to 32~~, wherein the sample is a tissue sample and the form or forms of Factor XIIa under investigation is/are detected or determined by immunohistology.

34. (currently amended) A method as claimed in claim 26 ~~claim 27 other than when dependent on claim 5~~, wherein the antibody is immobilized on a solid phase as a capture antibody.

35. (original) A method as claimed in claim 34, wherein the antibody immobilized on a solid phase as a capture antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

36. (currently amended) A method as claimed in claim 35, wherein the capture antibody is mAb 2/215 (ECACC 90011606) or an analogue thereof.

37. (currently amended) A method as claimed in claim 35, wherein the capture antibody is mAb 201/9 (ECACC 90012512) or an analogue thereof.

38. (currently amended) A method as claimed in claim 34~~any one of claims 34 to 37~~, wherein the solid phase is contacted with the sample and any resulting antigen-antibody complex is detected or determined using a labeled antibody ~~as defined in claim 28 or claim 29~~.

39. (original) A method as claimed in claim 38, wherein the labeled antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

40-42. Please cancel.

43. (currently amended) A method as claimed in claim 1 ~~any of claims 1 to 42~~, wherein the procedure enables preferential detection or determination of Factor αXIIa.

44. (currently amended) A method as claimed in claim 1 ~~any of claims 1 to 42~~, wherein the procedure enables preferential detection or determination of Factor βXIIa.

45-51. Please cancel.

52. (currently amended) A method as claimed in claim 1 ~~any of claims 1 to 42~~, wherein the ~~procedure enables preferential detection or determination of molecular complexes incorporating two or more molecules of Factor XIIa~~ form or forms of Factor XIIa under investigation is any one or more of complexes comprising two or more molecules of Factor XIIa, Factor XIIa associated with low affinity binding partners, and Factor XIIa associated with high affinity binding partners.

53-56. Please cancel.

57. (currently amended) A method as claimed in claim 1 ~~any one of claims 1 to 56~~, wherein the sample has been obtained from a subject having a disease or disorder, undergoing treatment for a disease or disorder, or after having had a disease or disorder or treatment for the disease or disorder.

58. (original) A method as claimed in claim 57, wherein the disease or disorder involves the coagulation system.

59. (original) A method as claimed in claim 57, wherein the disease or disorder involves hemaocoagulation, fibrinolysis, kininogensis, complement activation or angiogenesis, maintaining vascular wholeness and blood pressure, maintaining the constitutive anticoagulant character of the intravascular space, or tissue defence and repair.

60. (original) A method as claimed in claim 57, wherein the disease or disorder is or involves acute or chronic inflammation, shock of any aetiology including septic shock, diabetes, allergy, a thrombo-haemorrhagic disorder, sepsis, spontaneous abortion or an oncological disease.

61. (original) A method as claimed in claim 57, wherein the disease or disorder is or involves intravascular blood coagulation or thromboembolism, a myocardial infarction, acute coronary syndrome or angina.

62. (original) A method as claimed in claim 57, wherein the disease or disorder is or involves thrombosis or stenosis.

63. (original) A method as claimed in claim 57, wherein the disease or disorder is or involves suspected myocardial infarction or acute coronary syndrome.

64. (original) A method as claimed in claim 57, wherein the disease or disorder is or involves sepsis.

65. (original) A method as claimed in claim 57, wherein treatment involves administration of a therapeutic agent and/or involves a surgical procedure.

66. (original) A method as claimed in claim 65, wherein the treatment is coronary artery angioplasty or thrombolysis.

67. (currently amended) A method as claimed in claim 57 ~~any one of claims 1 to 66~~, wherein a series of samples obtained from a subject are tested.

68. (original) A method as claimed in claim 67, wherein samples are obtained during the course of the disease or disorder.

69. (currently amended) A method as claimed in ~~claim 66 or~~ claim 67, wherein samples are obtained during treatment of the disease or disorder, before treatment is started and/or after treatment has finished.

70. (original) A method for diagnosing, monitoring, or predicting the susceptibility to, progress of, or outcome of a disease or disorder, or of treatment of the disease or disorder in a subject having or suspected of having the disease or disorder, which comprises detecting or determining one or more forms of Factor XIIa in preference to other forms of Factor XIIa in a sample obtained from the subject, and comparing the results obtained for the subject with the results obtained using the same assay for samples obtained from at least any one or more of the following:
(i) subjects having the disease or disorder;
(ii) subjects having the disease or disorder, which subjects were monitored in relation to the progress and/or outcome of the disease or disorder;
(iii) subjects having the disease or disorder and the treatment;
(iv) subjects having the disease or disorder and the treatment, which subjects were monitored in relation to the treatment in relation to the progress and/or outcome of the disease or disorder;
(v) subjects who do not have the disease or disorder;
(vi) the same subject before the onset of the disease or disorder or before the start of the treatment of the disease or disorder; and
(vii) the same subject at an earlier or later stage of the disease or disorder or the treatment of the disease or disorder or before the onset of the disease or disorder.

71-74. Please cancel.

75. (currently amended) A method as claimed in claim 70 ~~or claim 71~~, wherein the sample is ~~samples are~~ from a ~~obtained upon or following admission of the~~ subject ~~to hospital~~ with suspected myocardial infarction, and wherein ~~low~~ levels of particular forms of Factor XIIa are associated with an increased risk of a secondary troponin positive event.

76. Please cancel.

77. (currently amended) A method as claimed in claim 70 ~~or claim 71~~, wherein the sample is ~~samples are~~ obtained from a ~~upon or following admission of the~~ subject ~~to hospital~~ with suspected myocardial infarction, and wherein ~~low~~ levels of particular forms of Factor XIIa are associated with an increased risk of death.

78. Please cancel.

79. (currently amended) A method as claimed in claim 70 ~~or claim 71~~, wherein high levels of particular forms of Factor XIIa are associated with sepsis.

80. (original) A method comprising carrying out a series of assays for Factor XIIa on samples obtained from subjects having a disease or disorder or treatment for a disease or disorder, and selecting an assay that provides information on Factor XIIa levels that is relevant to the disease or disorder or the treatment.

81. (original) A method for providing an assay for Factor XIIa suitable for providing information relevant for diagnosing, monitoring, or predicting the susceptibility to, progress of, or outcome of a disease or disorder, or of treatment of the disease or disorder in a subject having or suspected of having the disease or disorder, which comprises carrying out a series of assays for Factor XIIa on samples obtained from subjects having the disease or disorder or the treatment, and determining which assay(s) provide information on Factor XIIa levels that is relevant to diagnosing, monitoring, or predicting the susceptibility to, progress of, or outcome of the disease or disorder, or of treatment of the disease or disorder.

82. (original) A method as claimed in claim 81, comprising comparing the results obtained for Factor XIIa in the samples obtained from subjects having the disease or disorder otr the treatment with the results obtained using the same assay for samples obtained from at least any one or more of the following:

(i) subjects having the disease or disorder;

(ii) subjects having the disease or disorder, which subjects were monitored in relation to the progress and/or outcome of the disease or disorder;

(iii) subjects having the disease or disorder and the treatment;
(iv) subjects having the disease or disorder and the treatment, which subjects were monitored in relation to the treatment in relation to the progress and/or outcome of the disease or disorder;
(v) subjects who do not have the disease or disorder;
(vi) the same subject before the onset of the disease or disorder or before the start of the treatment of the disease or disorder; and
(vii) the same subject at an earlier or later stage of the disease or disorder or the treatment of the disease or disorder or before the onset of the disease or disorder.

83. (currently amended) A method as claimed in claim 70 ~~one of claims 80 to 82~~, wherein the assay is ~~a method as defined in any one of claims 1 to 56.~~ an immunoassay comprising an antibody immobilized on a solid phase as a capture antibody, wherein the capture antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa, wherein the solid phase is contacted with the sample and any resulting antigen-antibody complex is detected or determined using a labeled antibody, and wherein the labeled antibody is different from said capture antibody and is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

84-87. Please cancel.

88. (currently amended) A database comprising the results obtained according to a method as claimed in claim 80 ~~any one of claims 80 to 86~~.

89. Please cancel.

90. (original) A method for diagnosing or monitoring a disease or disorder, or monitoring treatment of the disease or disorder, which comprises detecting or determining Factor XIIa in the urine of a subject having or suspected of having the disease or disorder.

91. (original) A method as claimed in claim 90, wherein the disease is or involves renal function, renal disease or renal damage, or treatment therefore.

92-93. Please cancel.